



TITLE:

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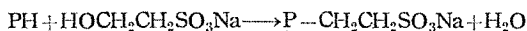
# Research upon Joint Reaction and Transjointing. (I)

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(Oda Laboratory)

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The authors have developed the idea of the Joint Reaction and Transjointing Reaction, about which the author had described already in this Bulletin. The authors have classified the Joint Reaction in three kinds and the Transjointing Reaction in four classes. Upon the Joint Reaction, the authors have in this paper reported the  $\beta$ -Sulfoethylation of various passive components. The reaction scheme can be expressed generally as follows :



As the passive components PH, the following compounds were used : diethyl malonate, ethyl acetoacetate, benzamide, phthalimide, oleyl- and stearyl-amide, carbazole, acetophenone and aniline. In each case the expected jointed product was obtained.

Upon the new types of Transjointing Reaction the authors have performed the following two experiments and have found that the Reaction can actually occur.

Transjointing between methylene-bis-acetoacetic ester and methylene-bis malonic ester.

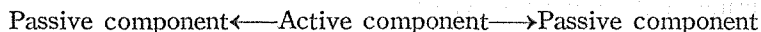
Transjointing between methylene-bis-malonic ester and methenyl-bis acetoacetic ester.

The authors have previously published a review<sup>1)</sup> about the Joint Reaction and Transjointing by formaldehyde, nitrous acid, phosgene and formic acid and about Transjointing reaction of the jointed compound by a third component. The authors have recently further developed the idea of Joint Reaction and Transjointing and at the same time performed some investigations and want to report here about the experimental results.

## I. Classification of the Joint Reaction

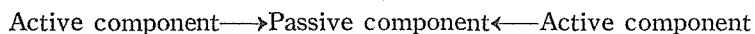
The authors have divided the Joint Reaction into the following three classes :

(a) Active Joint Reaction. Formaldehyde, nitrous acid, phosgene and formic acid are the typical active components<sup>2)</sup> and therefore joint two passive components.<sup>3)</sup> This type of Joint Reaction can be represented schematically as follows :



The authors want to call this type of Joint Reaction "Active Joint Reaction." Many examples were already given in the previous review and also many new examples have been published in recent foreign papers.<sup>23-27)</sup>

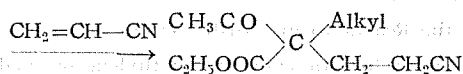
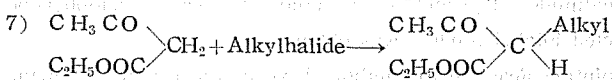
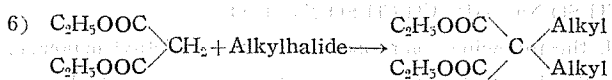
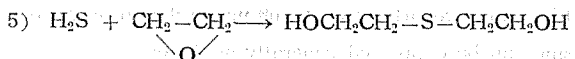
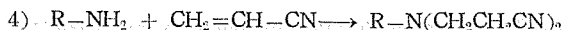
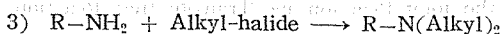
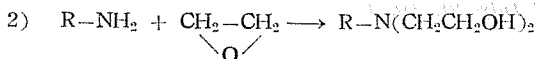
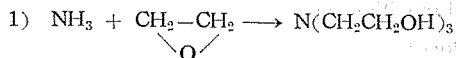
(b) There are many reactions, which are quite contrary to the Active Joint Reaction and can be called "Passive Joint Reaction." This type of Joint Reaction can be schematically represented as follows :



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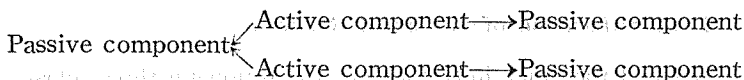
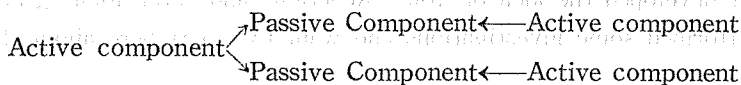
\* 小田良平, 寺村一広

Some examples of this type of Joint Reaction are given below, although they are very simple.



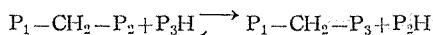
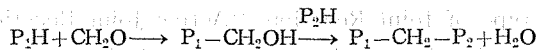
8) Preparation of polymethylol-compound by the reaction of  $\text{CH}_2\text{O}$  upon active-methyl compounds. etc.

(c) Mixed Joint Reaction. There should be many kinds of Joint Reaction, which are the mixed type of the above two Joint Reactions. This type of Joint Reaction can be schematically represented, for example, as follows :

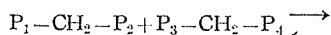
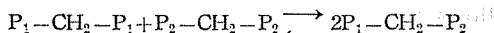


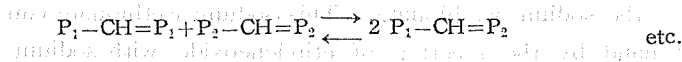
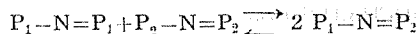
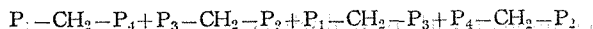
## II. Classification of Transjointing Reaction

(a) In the previous review the authors have chiefly given some examples of Transjointing of the following type :



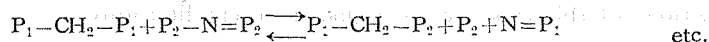
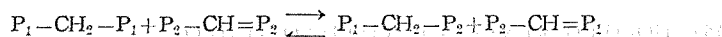
(b) The second type of Transjointing can be represented as follows:





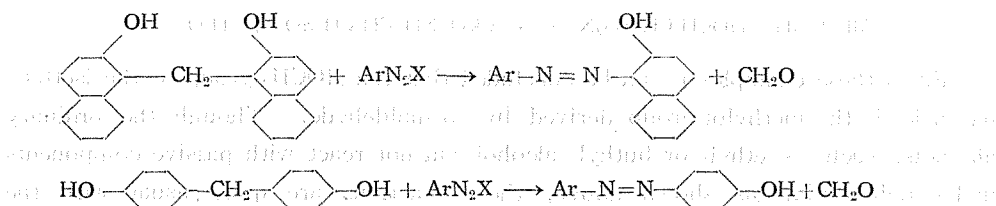
The Transjointing of type (a) corresponds to the alcoholysis or acidolysis of esters and that of type (b) corresponds to the trans-esterification between two different esters. But no research has been published about this second type of Transjointing. The authors have found a new example of this type, i. e. Transjointing can actually occur between methylene-bis-malonic ester and methylene-bis-acetoacetic ester, the result of which will be given in the the experimental part.

(c) Further the following type of Transjointing should exist.



Here, the  $P_1-CH_2-P_1$  is the jointed compound by formaldehyde,  $P_2-CH=P_2$  is the jointed compound by formic acid and  $P_2-N=P_2$  is the jointed compound by nitrous acid. There is no example of Transjointing of this type in the literature. The authors have found a new example, i. e. the Transjointing can actually occur between methylene-bis-malonic ester and methenyl-bis-acetoacetic ester. The results will be given in the experimental part.

(d) The fourth type of Transjointing can be deduced from the results of E. Ziegler's papers.<sup>39)</sup> The jointed phenols or naphthols by formaldehyde can be coupled by special diazo-compound as in the following examples.



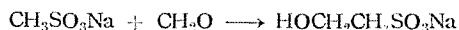
The resulted azo-compound is the jointed compound by nitrous acid and therefore this reaction can be seen as a type of Transjointing.

## EXPERIMENTAL PART

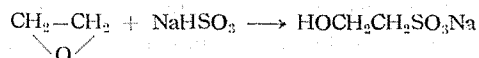
### I. $\beta$ -Sulfoethylation

It is a well-known fact, that the active-methyl- and active-methylene-compounds react with formaldehyde in the presence of basic catalyser and the corresponding methylol-compounds, are produced. The methane-sulfonic acid or its ester can be seen as a kind of active methyl-compound, but no one has ever

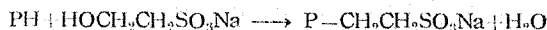
attempted to methylolize this compound with formaldehyde.



The product thus obtained is the sodium isethionate. This sodium isethionate can be prepared on the other hand by the reaction of ethyleneoxide with sodium-bisulfite.

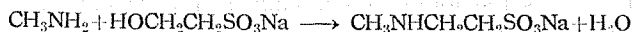


The methane-sulfonic acid is not easy to prepare and therefore the latter method is more convenient for the synthesis of isethionic acid in a large quantity. If the sodium isethionate is the methylolized product of methane-sulfonate with formaldehyde, it must joint the second passive component in the following manner :

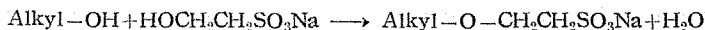


Indeed, some reactions of this type can be found in recent literature.

(a) Preparation of N-methyl-taurin from isethionic acid.



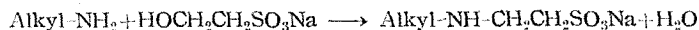
(b) Preparation of ether sulfonate, USP. 2,535,677, C. A. 45, 3408



(c) Reaction of isethionic acid with thiols, USP. 2,480,859, C. A. 44, 5778.



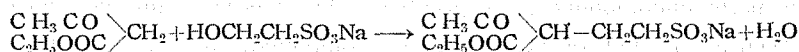
(d) Reaction of isethionic acid with higher alkylamines, USP. 2,658,072, J. Am. Oil Chem. Soc. 31, 168 (1954)



From these examples it can be concluded that the  $\text{HOCH}_2$ -group of the isethionic acid is the methylol-group derived by formaldehyde. Though the ordinary alcohols, such as ethyl- or buthyl- alcohol can not react with passive components under dehydration as shown above, these reactions are quite usual with the ordinary methylol-group produced by the reaction of formaldehyde.

The authors have attempted to synthesize the isethionic acid from methane-sulfonic acid and formaldehyde and the research is not yet complete, but the authors have prepared the isethionic acid on the other hand from ethyleneoxide and bisulfite and has succeeded in several new examples of Joint Reaction, by reacting this isethionic acid with various passive components. The experiments performed are as follows :

(1) Reaction with acetoacetic ester.



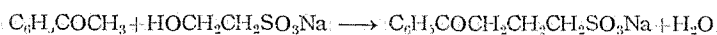
In a flask, equipped with thermometer, stirrer and reflux air condenser, acetoacetic ester (150 g), Na-isethionate (10 g), and anhydrous  $\text{ZnCl}_2$  (20 g) were mixed. The flask was then heated in oil bath and refluxed under stirring. The content of the flask soon became reddish and then dark-reddish. After about 4 hrs. the content was hot filtered, the residue was treated again with hot ester and the filtrates were mixed together. Then the excess ester was recovered by vacuum distillation and the residue was recrystallized twice from alcohol and dried. The product was analyzed as the aimed  $\beta$ -sulfoethyl-acetoacetic ester and the yield was 5,6 g (32%). This compound is hygroscopic and soluble easily in water and exhibits with  $\text{FeCl}_3$  a remarkable purple-reddish colour. An analogous result was obtained, using Na-ethoxylate as catalyser.

(2) Reaction with diethyl malonate.



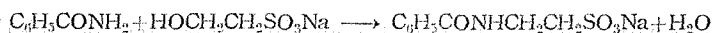
By the analogous method as above the aimed  $\beta$ -sulfoethyl-malonate was obtained in 23 % yield of the theory.

(3) Reaction with acetophenone.



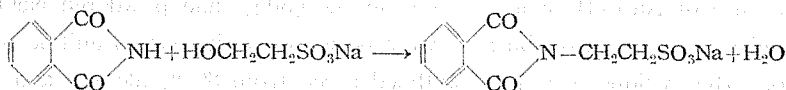
Acetophenone (25 g.) and Na-isethionate (10 g) were mixed and heated in oil bath up to  $190^\circ$  and the mass was melted. Next powdered NaOH (0.3 g) was added and the heating was continued. The content became soon reddish and solidified. After further 2 hrs. heating without stirring the cooled mass was crushed, extracted with boiling water and hot filtered. By cooling the filtrate the aimed  $\gamma$ -benzoyl-propanesulfonate was obtained in 41 % yield of the theory.

(4) Reaction with benzamide.



In a flask, equipped with thermometer, stirrer and reflux air condenser, benzamide (12 g) and Na-isethionate (12 g) were mixed and heated in oil bath up to  $180-190^\circ$  and the mass was melted. Next powdered NaOH (0.3 g) was added and the temperature was raised to  $210-220^\circ$ . After about 2 hrs. heating at this temperature the content was solidified. After cooling the mass was crushed and extracted with hot water. The product, separated from the filtrate after cooling, was recrystallized twice from 80% alcohol. The yield of the pure N-benzoyltaurin was 7 g (40%).

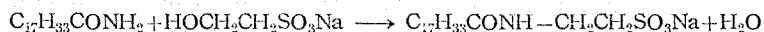
(5) Reaction with phthalimide.



By the analogous method as above the aimed N-( $\beta$ -sulfoethyl)-phthalimide

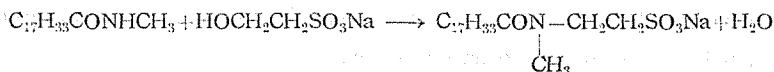
was obtained in 50.4 % yield of the theory.

(6) Reaction with oleylamide and stearylamine.

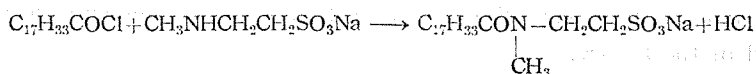


By the analogous method as above the aimed N-( $\beta$ -sulfoethyl)-oleylamide and stearylamine were obtained respectively in 23 % and 30 % yield of the theory.

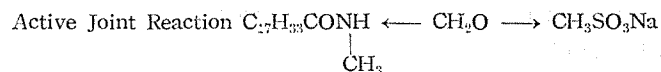
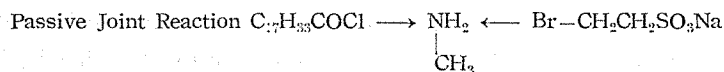
The products here obtained are the Igepon-like surfactants and when the N-methyl-oleylamide is used instead of the oleylamide, the Igepon T itself can be obtained.



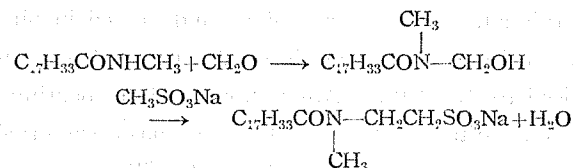
Thus the authors have found a new synthetic method of Igepon T, using the idea of the Joint Reaction. The Igepon T has been synthesized practically through the following course :



When this ordinary synthetic method of Igepon T is compared with the new method, which the authors have here established, a very interesting contradistinguishable fact is found, that is, the former method is based on the Passive Joint Reaction and the latter new method on the Active Joint Reaction, represented schematically as follows :



It is also noticeable that the Igepon T could be synthesized through the following course :

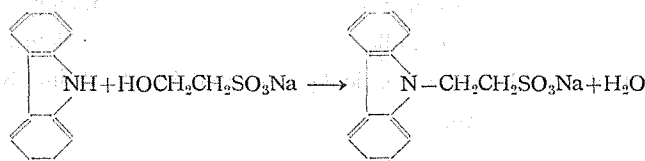


(7) Reaction with aniline.



A mixture of Na-isethionate (20 g), aniline (50 g) and powdered NaOH (0.3 g) was heated five hours in oil bath. After removal of the excess aniline by vacuum distillation, the residue was recrystallized twice from 80 % alcohol and the aimed N-phenyltaurin was obtained in 60 % yield of the theory.

## (8) Reaction with carbazole.



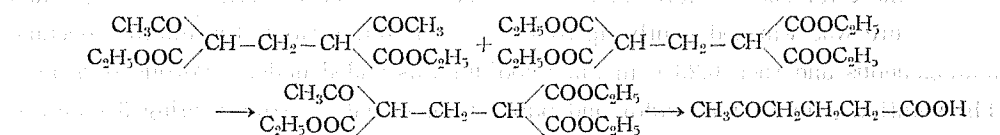
A mixture of carbazole (5 g) and Na-isethionate (15 g) was heated in oil bath up to 220-230° and to this molten mass 0.1 g powdered NaOH was then added. The mass solidified soon. After cooling it was extracted by hot water without insoluble residue. From this solution separated out the product and after recrystallization from water it was analyzed as the N-(β-sulfoethyl)-carbazole.

As has been mentioned above, the carbazole reacts very easily with Na-isethionate and produces water-soluble N-(β-sulfoethyl)-carbazole and the anthracene does not react perfectly with Na-isethionate, this procedure can be utilized as a useful method of separating anthracene from carbazole. The authors have experimentally proved this fact, i. e. from a mixture of anthracene and carbazole only carbazole was solubilized out, left remaining the pure anthracene.

## II. Some Researches upon Transjointing

## (1) Transjointing of the type (a).

Transjointing between methylene-bis-acetoacetic ester and methylene-bis-malonic ester.



In a flask, equipped with thermometer, stirrer and reflux condenser, methylene-bis-acetoacetic ester (27.2 g) and methylene-bis-malonic ester (33.2 g) were mixed and into this mixture 0.23 g metallic sodium was added. Soon after the addition of sodium the solution became pink-colored. After standing at room temperature for two hours the content of the flask was heated in a boiling water bath. The sodium disappeared gradually and the color of the solution changed from pink to yellowish orange. After two hours heating the solution was neutralized with acetic acid and washed with water. The oily product which had sunk below water, was separated and dried with Na<sub>2</sub>SO<sub>4</sub> and distilled under vacuum.

First fraction 60-80°/5mm. 7 g.

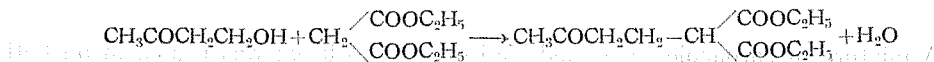
Chief fraction 150-165°/5mm 23 g.

Residue 7 g.

By redistillation of the chief fraction, the fraction boiling at 160-165°/5 mmHg was collected (15.5 g). This fraction was next refluxed with two-fold quantity of



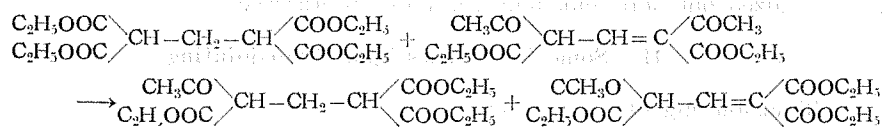
50 % alcoholic hydrochloric acid for 12 hours in water bath and after removal of alcohol the residue was extracted with ether and fractionated again under vacuum. The main fraction (115-116.5/2mm) was collected. This fraction is identical with  $\gamma$ -acetyl- $\alpha$ -carbethoxy-butyric ethylester, autentically prepared by the Joint Reaction of  $\gamma$ -ketobutanol with diethyl malonate.



This  $\gamma$ -acetyl- $\alpha$ -carbethoxy-butyrate fraction was further hydrolyzed under heating with two-fold quantity of 1 : 1 - hydrochloric acid for five hours and extracted with ether. By fractional distillation of the ether solution the fraction (135-136°/5mm) was collected in 35 % yield and it was identified as  $\gamma$ -acetyl-butyric acid, deriving it to the semicarbazone. m. p. 170~171°C, no depression with the authentic sample.

## (2) Transjointing of type (c).

Transjointing between methylene-bis-malonic ester and methenyl-bis-acetoacetic ester.



In a flask, equipped with thermometer, stirrer and reflux condenser, methylene-bis-malonic ester (35 g) were mixed with methenyl-bis-acetoacetic ester (27 g) and the mixture was warmed gently up to 70°. At this temperature the mixture became homogeneous and then 0.23 g metallic sodium was added under vigorous stirring. The solution exhibits pink color and bubbles somewhat. After heating 5 hours at 80~90°, the temperature was raised to 120° and maintained at this temperature for further 5 hours. After cooling and neutralized with acetic acid, the product was extracted with ether. The ether solution was washed with water, dried with  $\text{Na}_2\text{SO}_4$  and fractionally distilled.

First fraction 60~100°/5mm

2 g.

Chief fraction 155~165°/5mm

30 g.

Residue

ca. 10 g.

From this chief fraction, the  $\gamma$ -acetyl-butyric acid was detected after hydrolyzing as in the case (1) and introducing it to the semicarbazone.

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